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10/551,466	08/07/2006	Ji Hoon Jeong	2229.0020000/JUK/SMW	4435

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EXAMINER

WHITEMAN, BRIAN A

ART UNIT	PAPER NUMBER
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1635

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05/17/2011

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/551,466	Applicant(s) JEONG ET AL.	
	Examiner BRIAN WHITEMAN	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 March 2011.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4 and 6-14 is/are pending in the application.
- 4a) Of the above claim(s) 11-14 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4,6-10 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>1/19/11</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Brian Whiteman, Art Unit 1635.

Election/Restrictions

Claims 11-14 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 11/15/07.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 4, 6, 7, 9, and 10 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Hoffman, et al. (US Patent 7,737,108, filed 01/05/2001).

The claims are directed to a conjugate for gene transfer wherein the conjugate comprises an antisense oligonucleotide and a hydrophilic polymer, such as PEG, wherein the polymer is covalently attached to the end of the oligonucleotide by an acetal bond. Claims 9 and 10 are directed to a product-by-process wherein the product is the same as that claimed in claim 1, an antisense oligonucleotide-polymer conjugate.

Hoffman et al. teach antisense oligodeoxynucleotides linked to a hydrophilic polymer such as PEG by an acetal bond (column 4, lines 27-34 and lines 46-51). Oligodeoxynucleotides comprise deoxyribonucleosides linked by phosphodiester bonds. Hoffman, et al. exemplify the use of PEG having a molecular weight of 5kD (column 21, lines 66-67). Hoffman et al. do not specifically teach that the polymer is attached to an

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end of the oligonucleotide or that the polymer conjugated to the oligonucleotide has a molecular weight of over 500 Daltons.

It would have been obvious to one of skill in the art at the time of the instant invention to make an antisense oligonucleotide conjugated to PEG via an acetal bond because Hoffman et al. teach such a conjugate. It would have been obvious to attach the PEG to an end of the oligonucleotide because the ends of the oligonucleotide are free (i.e., not attached to another nucleotide). It further would have been obvious to use PEG that has a molecular weight that is greater than 500 Daltons because Hoffman, et al. exemplify the use of PEG having a molecular weight of 5000 Daltons. Therefore, the claims would have been obvious at the time the instant invention was made.

Response to arguments

Applicant's arguments filed 3/17/11 have been fully considered but they are not persuasive.

In response to applicant's argument that the amended claim 1 does not include a hydrophobic component as an essential component, the argument is not found persuasive because the term "consisting essential of" does not limit the scope of the claims to the specified material of the claimed invention. See *In re Herz*, 537, F. 2d 549, 551-52, 190 USPQ 461, 463 (CCPA 1976). "If an applicant contends that additional steps or materials in the prior art are excluded by the recitation of "consisting essentially of," applicant has the burden of showing that the introduction of additional steps or components would materially change the characteristics of applicant's invention." See *In re De Lajarte*, 337 F.2d 870, 143 USPQ 256 (CCPA 1964). See also

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Ex parte Hoffman, 12 USPQ2d 1061, 1063-64 (Bd. Pat. App. & Inter. 1989). The claimed invention and the product made obvious by the prior art can both be used for delivering an antisense oligonucleotide to a cell line. The applicant has not shown that the additional component would materially change the characteristics of applicants' invention. In the absence of a clear indication in the specification or claims of what the basic and novel characteristics actually, "consisting essentially of" will be construed as equivalent to "comprising". See MPEP 2111.03.

In response to applicant's argument that one of ordinary skill in the art would not have looked at Hoffman and predicted the result of the present invention the argument is not found persuasive because the claimed invention is directed to a product not a method of using the product. It would have been obvious to one of ordinary skill in the art to try and make the claimed product and have a reasonable expectation of success of making the claimed product. "The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." See **KSR v. Teleflex**, 550 U.S. 398, 127 S. Ct. 1727 (2007).

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Claims 1-4 and 6-10 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Hoffman, et al. (US Patent 7,737,108, filed 01/05/2001, of record) as applied to claims 1, 2, 4, 6, 7, 9, and 10 above, and further in view of Tullis (1990, US Patent 4,904,582, of record).

Claims 1, 2, 4, 6, 7, 9, and 10 are described above. Claim 8 is to a conjugate for gene transfer comprising a hydrophilic polymer and an antisense oligonucleotide comprising a nucleotide sequence complementary to a portion or entire nucleotide sequence of the c-myc gene.

Hoffman et al. render claims 1, 2, 4, 6, 7, 9, and 10 obvious for the reasons presented in the preceding rejection. Hoffman, et al. does not teach the antisense oligonucleotide-hydrophilic polymer conjugate wherein the antisense oligonucleotide is complementary to a portion or to the entire nucleotide sequence of the c-myc gene (instant claim 8) or wherein the antisense oligonucleotide has a molecular weight ranging from 1000-50000 daltons (instant claim 3).

Tullis describes oligonucleotide conjugates for transport across cellular membranes for modulating gene expression (abstract). In Table 1 in column 19, Tullis discloses the "MBF 20 antisense C₂-PEG" probe that comprises a 20-nucleotide phosphodiester-linked molecule conjugated to PEG (M_r= 3500). Such a probe is complementary to a portion of the c-myc gene. Tullis teaches that the PEG group can be added to 5'- or 3'-end of the antisense oligonucleotide by various protocols (column 5, line 44 to column 6 line 8). According to the website, www.newton.dep.anl.gov (of record), a 20-nucleotide single-stranded DNA molecule has a molecular weight of approximately 6600 daltons (330 daltons per nucleotide).

It would have been obvious to one of skill in the art at the time the instant invention was made to make an antisense-PEG conjugate wherein the antisense oligonucleotide comprises a sequence that is complementary to a portion of the c-myc

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gene and wherein the PEG is conjugated to the oligonucleotide via an acetal bond because Tullis, et al. teaches antisense oligonucleotide-PEG conjugates wherein the oligonucleotide comprises a sequence having complementarity to a portion of the c-myc gene and Hoffman et al. teach that antisense oligonucleotides can be conjugated to PEG via an acetal bond.

Response to arguments

Applicants do not provide any additional arguments that require addressing by the office and the office has already addressed any pertinent arguments in the previous rejection.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422

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F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 2, 3, 4, 6, 7, 8, 9, and 10 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3, 8, 10, and 13 of copending Application No. 11/651,011 in view of Hoffman, et al. (US Patent 7,737,108, of record)

The instant claims are directed to a composition comprising an oligonucleotide and a hydrophilic polymer wherein an end of the oligonucleotide is covalently linked to the hydrophilic polymer via an acid-cleavable linkage, which is an acetal bond. Claim 4 specifies that the hydrophilic polymer can be PEG. Claim 2 specifies that the hydrophilic polymer has a molecular weight of over 500 daltons. Claim 3 specifies that the oligonucleotide has a molecular weight ranging from 1000 to 50000 daltons. Claims 7 and 8 specify that the oligonucleotide is a c-myc-targeted antisense oligonucleotide.

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The claims of the 11/651011 application are directed to a composition comprising a c-myc-targeted siRNA and a hydrophilic polymer (PEG) wherein an end of the siRNA is covalently linked to a hydrophilic polymer via an acid-cleavable linkage. The siRNAs encompassed by the '011 claims include those having a molecular weight of 10,000 to 30,000 (paragraph 15) and the PEG of the '011 claims includes that having a molecular weight of between 1000 to 10,000 (see original claim 2 of the '011 application). The '011 claims and specification do not specify that the acid cleavable linkage is an acetal bond.

Hoffman teaches conjugation of antisense oligonucleotides and PEG via an acetal bond.

The instant claims would have been *prima facie* obvious to one of skill in the art provided with the claims of the 11/651,011 application and the teachings of Hoffman, et al. Aside from the limitation of an acetal bond in the instant claims, the siRNA-PEG complex of the '011 application is a species of the instantly claimed oligonucleotide-PEG complex. Hoffman, et al. provide the teaching that an acetal bond is a preferred acid-cleavable linkage for conjugating PEG and oligonucleotides (see rejection under 35 USC § 103, above) such that one of skill in the art would recognize that the acid-cleavable linkage specified in the '011 claims include an acetal bond and that such a bond is preferred, according to Hoffman. One of skill in the art would also recognize that the c-myc-targeted siRNA of the '011 application claims could be substituted with the instantly claimed c-myc-targeted antisense oligonucleotide because both molecules are known gene expression inhibitors. Therefore, the instant claims would have been

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prima facie obvious to one of skill in the art provided with the '011 claims and the teachings of Hoffman.

This is a provisional obviousness-type double patenting rejection.

Applicant's arguments filed 3/17/11 have been fully considered but they are not persuasive because applicant did not address the provisional double patenting rejection. It is noted that applicant request the provisional rejection be held in abeyance until allowable subject matter in the present application or co-pending application No. 11/651,011 is indicated.

Claims 1-4 and 6-10 are directed to an invention not patentably distinct from claims 1, 3, 8, 10 and 13 of commonly assigned US 11/651,011. Specifically, for the reasons set forth in the provisional double patenting rejection.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned co-pending US application, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number 571-272-0764. The examiner can normally be reached on Monday-Thursday from 6:30 to 4:00 (Eastern Standard Time). The examiner can also be reached on alternate Fridays.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Heather Calamita can be reached on 571 272-2876. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Brian Whiteman/

Primary Examiner, Art Unit 1635